UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/604,943	08/28/2003	Itzhak Bentwich	050992.0300.07USCP	1942

37808 7590 05/29/2008

ROSETTA-GENOMICS
c/o PSWS
700 W. 47TH STREET
SUITE 1000
KANSAS CITY, MO 64112

EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
05/29/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/604,943	BENTWICH, ITZHAK	
	Examiner	Art Unit	
	DANA SHIN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21,23,35,36,38 and 39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,23,35,36,38 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4-21-08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

This Office action is in response to the communications filed on April 21, 2008.

Currently, claims 21, 23, 35-36, and 38-39 are under examination on the merits.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections

Priority

The benefit of the 60/441,241 filing date remains denied in the instant case for the reasons of record as set forth in the Office action mailed on November 20, 2007 and for the reasons stated below. Applicant's arguments filed on April 21, 2008 have been fully considered but they are not persuasive. Applicant argues that the disclosure of 60/363,124 also contains CDs containing SEQ ID NOs:128, 131, 133, 477, 480, and 482 and submitted the cover sheet. Applicant's attention is directed to the fact that it is clearly made of record that not all CDs

submitted were not received by the Office as clearly indicated on the cover letter. Furthermore, there is no record of those SEQ ID NOs in the application file of 60/363,124. Hence, the benefit of an earlier filing date remains denied for all pending claims in the instant application.

Claim Rejections - 35 USC § 101

Claims 21, 23, and 35-36 remain rejected under 35 U.S.C. 101 as lacking a specific and substantial asserted utility or a well established utility for the reasons of record as set forth in the Office action mailed on November 20, 2007 and for the reasons stated below.

Applicant's arguments filed on April 21, 2008 have been fully considered but they are not persuasive. Applicant argues that the claimed miRNA-related SEQ ID NOs are specific because they modulate expression of "specific" gene transcripts such that SEQ ID NO:477 targets "ACADSB"; SEQ ID NO:482 targets "ZNF36"; and SEQ ID NO:480 targets "INHBA". Contrary to applicant's argument that each SEQ ID NO specifically modulates a specific gene transcript, there is no evidence in the specification as originally filed showing that any of the claimed nucleotide sequences specifically binds and modulates the allegedly "specific" target transcripts in actuality. For instance, there is no showing or evidence that SEQ ID NO:482 indeed specifically modulates "ZNF36". Applicant has named the precursor miRNA for SEQ ID NO:482 as "GAM147" and postulated that it has binding sites for 11 different target genes. For instance, Table 2 filed on August 28, 2003 discloses the following 11 genes as potential target/binding genes for "GAM147" comprising SEQ ID NO:482, one of which is "ZNF36". See below:

GAM147	ATP10C	3'	AATACAGGAAACAAGAGGTAC	2062	T __ GT CCTC GTTTCCTGTATT || |||| |||||||||||| CA GGAG CAAAGGACATAA
GAM147	CASP10	3'	ACAGGGAACAAAGAAACA	2304	T AA C C_ TGTT CT GTTTCCTGT |||| || |||||||| ACAA GA CAAGGGACA
GAM147	ZNF36	3'	GGAAACAGAAACATAGA	3627	A AA C C TCTATGTT CT GTTTCC |||||||| ||| |||||| AGATACAA GA CAAAGG
GAM147	DORFIN	3'	AATACAGGAAATAGATAAACAT G	1630	A _ CC _ TATGTT TC GTTTCCTGTATT |||||| || |||||||||||| GTACAA AG TAAAGGACATAA
GAM147	FLJ21313	3'	AATACAGGATGAAAAACACTGA	2037	AT A TA CC TT TC TGTT TCG TCCTGTATT || |||| ||| |||||||||| AG ACAA AGT AGGACATAA
GAM147	KIAA1819	5'	AATACAGGAGATAGAACCAGA	2865	TC AA __ AT CTC TCT GTTC GTTTCCTGTATT ||| |||| |||||||||||| AGA CAAG TAGAGGACATAA
GAM147	P37NB	3'	ATGGGAAAAAAAAACATAGA	1254	C_ A__ CCTCG TCTATGTT TTTCCTGT ||||||||| |||||||| AGATACAA AAAGGGTA
GAM147	RAP140	5'	ATACAGATAGAAACATAGA	1613	AAA__ CC GTTTC TCTATGTT TC CTGTAT ||||||||| || |||||| AGATACAA AG GACATA
GAM147	LOC127002	3'	AATATAAAAACAGAAACATAGA	3002	__ ATA__ C C CC TCTATGTT CT GTTT TGTATT ||||||||| || |||| |||||| AGATACAA GA CAAA ATATAA
GAM147	LOC132332	3'	AATACAGTTGCAGAGGAGCATA	3046	A _ A_ _ TTC TATGTTCCTC GT CTGTATT ||||||||||| || ||||||| ATACGAGGAG CG GACATAA
GAM147	LOC145624	5'	ACTAGAAGAGGAACATA	3276	A TT_ GT CT TATGTTCCTC TTC GT ||||||||||| ||| || ATACAAGGAG AAG CA

It is unclear why applicant chose "ZNF36" to argue for the utility of the claimed miRNA sequence comprising SEQ ID NO:482. Nevertheless, applicant has failed to show that the purported utility of modulating any one of 11 genes listed above is indeed specific for SEQ ID

NO:482. As such, the utility issue in the instant case is no different from the lack of utility of the EST sequences of *In re Fisher*. Since there is no factual evidence that the claimed nucleotide sequences bind and modulate their respective, specific target genes that are not even disclosed in the specification, it is concluded that the claimed SEQ ID NOs do not have a specific utility.

Applicant further argues that the claimed SEQ ID NOs have a substantial utility because the targeted transcripts have known functions unlike the ESTs of *In re Fisher*. Applicant asserts that ACADSB was known to be a member of the acyl-CoA dehydrogenase family and that it was known to react with 2-methylbranched chain substrates; INHBA was known to encode βA and various functions were known; and ZNF36 was "predicted" to encode a protein belonging to the Kruppel family of zinc finger proteins, and therefore, the claimed nucleic acids have a substantial utility because they "may be used to bind and regulate mRNA transcripts of INHBA, ZNF36, or ACADSB". Contrary to applicant's assertions, the claimed miRNA-related sequences have not been shown to bind and modulate the alleged target transcripts. Hence, whether or not the functions of INHBA, ZNF36, and ACADSB were known is irrelevant because the claimed nucleotide sequences were not known or described to indeed bind and modulate the alleged genes, ACADSB, INHBA, and ZNF36, and moreover, the sequences were not verified as miRNA sequences. In addition, contrary to the characteristics of the "invention" such that the claimed nucleotide sequences are miRNAs that are "viral regulatory RNA genes" (see paragraph 0009), further evidenced by the sequence listing identifying the "organism" for SEQ ID NOs: 477, 480, and 482 as "Vaccina Virus", applicant is arguing that the claimed nucleotide sequences modulate the functions of ACADSB, INHBA, and ZNF36, none of which are viral genes. As such, applicant has failed to show that the claimed nucleic acids are substantially useful (that is,

having a "real world" use), especially in the context of the spirit of the invention (e.g., viral regulatory miRNA). Again, note that the specification as originally filed does not provide any description/support that the claimed nucleotide sequences in the instant case are truly miRNA sequences, let alone they bind and modulate their respective target transcripts, which are in the instant case alleged to be ACADSB, INHBA, and ZNF36. In order to comply with the substantial utility, "[A]n application must show that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research. Simply put, to satisfy the substantial utility requirement, an asserted use must show that the claimed invention has a significant and presently available benefit to the public." *Fisher*, 421 F.3d at 1371, 76 USPQ2d at 1230. In addition, MPEP §2107.01 teaches the following: "substantial utility" defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

Applicant further asserts that the claimed invention has a credible utility and the claimed nucleic acids "must be operable to achieve useful results". Applicant also states that the "proper inquiry" for determining credible utility is the question of "more than likely than not true". As stated above, applicant has not provided any logical reasoning or preponderance of evidence as to why the claimed nucleic acids will function, more likely than not, as "viral regulatory RNA genes" or "miRNAs" that bind and modulate ACADSB, INHBA, and ZNF36. In fact, applicant has not provided any factual, probative evidence showing that the claimed nucleotide sequences will be "operable to achieve useful results" such as modulating the functions of ACADSB, INHBA, and ZNF36. Applicant further asserts that the expert testimony in the field of miRNA

submitted as the declaration is sufficient to overcome this rejection. Contrary to applicant's assertions, the declaration under 37 CFR 1.132 filed on April 21, 2008 is insufficient to overcome the rejection of claims 21, 23, and 35-36 based upon the lack of utility as set forth in the last Office action because the mere listing of SEQ ID NOs:477, 480, and 482 in Table A does not reflect any credible utility for the claimed nucleic acids, nor the listing of a few of previously identified miRNA sequences provides evidence that the instantly claimed nucleic acids have a credible utility as viral regulatory genes or miRNAs that bind and modulate target transcripts. Further, the declaration does not provide any substantial statement, let alone evidence, that one of ordinary skill in the art would have immediately seen the utility of the instantly "claimed" nucleic acids based on the disclosure of the specification and general knowledge in the art. Since neither the declaration nor applicant's arguments demonstrate that the claimed nucleic acids will "be operable to achieve useful results", it is concluded that the claimed invention lacks a credible utility. Note also that applicant states "The Pilpel Declaration indicates that a nuclei acid having the sequence as set forth in SEQ ID NO:477 or SEQ ID NO:480 or SEQ ID NO:482 has been biologically validated.", which is entirely false. Nowhere in the declaration does the declarant state that any one of the instantly claimed SEQ ID NOs has been "biologically validated". In the next reply, applicant is required to point out the specifics from the declarant's statement wherein he indicates such findings as alleged by applicant.

In addition, the declaration (Table A) provides all the more reasons why the claimed nucleic acids do not have a credible utility or a well established utility. As clearly disclosed in Table A of the declaration, none of the claimed SEQ ID NOs in the instant case has a credible or a well established utility because none of them has been verified or validated by artisans in the

miRNA field. For example, SEQ ID NO:354 of Application No. 10/707,147 has been validated as a valid miRNA sequence, which has been subsequently identified and known in the art as "has-miR-196b" (see page 3), whereas none of the claimed SEQ ID NOs has yet to be validated as a valid miRNA sequence (see pages 6-7). Hence, the claimed nucleic acids are no more than purported, speculative nucleic acid sequences, which are merely alleged by applicant of the instant application to be valid miRNA sequences.

In the instant case, the specification fails to disclose enough information about the invention to make its usefulness immediately apparent to those familiar with the technological field of the invention. In view of the foregoing, the claims remain rejected as failing to comply with the utility requirement.

Claim Rejections - 35 USC § 112

Claims 21, 23, and 35-36 remain rejected under 35 U.S.C. 112, first paragraph for the reasons of record as set forth in the Office action mailed on November 20, 2007 and for the reasons stated below.

Applicant's arguments filed on April 21, 2008 have been fully considered but they are not persuasive. Applicant argues that since the claims comply with the utility requirement, they also comply with §112, first paragraph. As indicated above, the claims do not comply with the utility requirement. Hence, this rejection is maintained.

New Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims are drawn to a probe comprising SEQ ID NO:128, 131, 133, 477, 480, or 482.

Applicant has pointed out original claims 12-14 in support of the new claims. Claim 12 recites "A probe comprising the DNA of claim 1" as originally filed on August 28, 2003, wherein claim 1 recites a "bioinformatically detectable novel viral gene". However, there doesn't appear to be a written description of the claimed probe comprising SEQ ID NO:128, 131, 133, 477, 480, or 482, wherein SEQ ID NO:128, 131, 133, 477, 480, or 482 is a " viral gene" in the application as originally filed. That is, there is no description that any of the nucleotides claimed in the instant case is a "viral gene" as stated above for the utility rejection, nor there is an adequate support that the inventor, at the time of the original filing, contemplated of making a probe for SEQ ID NOs:128, 131, 133, 477, 480, or 482, wherein each recited SEQ ID NO is a "viral gene". Accordingly, the claims contain new matter which is not adequately described in the application as originally filed.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

/J. E. Angell/
Primary Examiner, Art Unit 1635